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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/576,858	05/22/2000	Richard O. Snyder	40447	2597

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EXAMINER
PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
1632	16

DATE MAILED: 03/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.	Applicant(s)
09/576,858	Snyder et al.
Examiner	**Art Unit**
Scott D. Priebe, Ph.D.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Feb 28, 2002* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) X The period for reply expires *3* months from the mailing date of the final rejection.

b) In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.

3. X The proposed amendment(s) will not be entered because:

   (a) X they raise new issues that would require further consideration and/or search. (See NOTE below);

   (b) X they raise the issue of new matter. (See NOTE below);

   (c) X they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) X they present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: *see following pages*

4. Applicant's reply has overcome the following rejection(s):

5. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).

6. X The a) affidavit, b) exhibit, or c) X request for reconsideration has been considered but does NOT place the application in condition for allowance because:
   see following pages

7. X The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

8. X For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):

   Claim(s) allowed: *none*

   Claim(s) objected to: *none*

   Claim(s) rejected: *1, 4, 7, 15, 16, 20, 26, 27, 31, 32, 36, 39, and 43*

9. The proposed drawing correction filed on _____ a) has b) has not been approved by the Examiner.

10. Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ .

11. X Other: *see following pages*

SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER
ART UNIT 1632

Advisory Action

Continuation of Item 3:

The scope of claim 1, and claims dependent therefrom, has been dramatically changed. Pending claim 1 is directed to expression of a polynucleotide in a mammal involving administration of either rAAV particles to liver cells in the mammal or cells infected with rAAV to the liver via the hepatic portal vasculature (in claim 4 only). However, proposed claim 1 is directed to a method for providing *liver specific expression* by administration of rAAV to mammalian cells (not only liver cells), the claim do not require the cells to be in or end up in a liver or a mammal. For example, proposed claim 1 reads on treating an isolated sample of liver tissue. Claim 1 recites "therapeutic gene" and "regulatory region for gene expression in *human* liver cells". Applicant has not indicated where the first term is supported by the specification, and the pages cited as supporting the second, do not. It is also unclear where the specification supports a method for "providing liver specific expression" as it is broadly as claimed in the proposed claims. In addition, due to the proposed amendment to claim 1, terms in some dependent claims no longer have antecedent basis, e.g. "said mammal" in claim 16. The extensive broadening of the claim being proposed raises new issues under §112, 1st para., both the enablement and written description requirements, §112, 2nd para. and under §102 and §103, requiring new search and consideration.

In additions, proposed claims 7, 15, 27, 31, 36, 43, 58-61, 63-65, and 68-70 all include new narrow limitations on one or more elements. This proposed narrowing of claims raises new

issues under §112, 1st para., enablement requirement, §102, and §103, requiring new search and consideration.

In addition, the amendment as filed does not comply with the requirements of 37 CFR 1.121(b)&(c), and cannot be entered as filed. Applicant has not provided a clean version of the paragraphs or pages amended, specifically the proposed amendments to pages 36 and 39, and the marked-up version does not clearly indicate the changes. The marked-up version of the proposed claim amendments is illegible and cannot be properly interpreted. Applicant is urged to provide a type-written marked-up version of proposed claims which clearly indicates the changes being made.

Continuation of item 6:

With respect to the rejection under §112, 1st para., the arguments are based on the exhibits which are not being considered (see item 7). With respect to the rejection under §112, 2nd para. and the rejections under §102; the arguments are predicated on entry of the proposed claims, which have not been entered. Also, proposed claim 1 does not recite that the "regulatory region" is liver-specific, only that it express in human liver cells. General promoters such as the CMV IE promoter and MLV LTR promoter do function in liver cells. Furthermore, there is no evidence of record that β-globin is not a therapeutic protein. A deficiency in β-globin causes β-thalassemia. Simply because the instant specification does not include it in one of its laundry lists of therapeutic proteins does not mean that it is not. Even if the proposed claims had limited the

regulatory region to one being liver-specific, this would have raised an additional new issue for search and consideration under 35 USC 103.

Continuation of item 11.

The information disclosure statements filed 2/21/02 and 2/28/02 fail to comply with 37 CFR 1.97(d) because they lack a statement as specified in 37 CFR 1.97(e). The information disclosure statement filed 2/28/02 fails to comply with 37 CFR 1.97(d) because it lacks the fee set forth in 37 CFR 1.17(I). The information disclosure statements have been placed in the application file, but the information referred to therein has not been considered.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry concerning administrative, procedural or formal matters relating to this application should be directed to Patent Analyst Patsy Zimmerman whose telephone number is (703) 308-8338. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.